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# Efficacy of Airway Pressure Release Ventilation in treating acute respiratory distress syndrome

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## ABSTRACT

*Background:* Acute respiratory distress syndrome (ARDS) is a serious condition which necessitates admission to an intensive care unit, is linked to a high rate of hospital death. Refractory hypoxemia is the most significant pathophysiological characteristic of ARDS. Airway pressure release ventilation (APRV) characterized as a constant positive airway pressure with intermittent release phase. It also has a good effect in patient with acute respiratory distress syndrome (ARDS) therapy paradigm. This study set out to assess the effectiveness of APRD in raising oxygenation levels and reducing death rates in severely ill ARDS patient. *Method:* The study was carried out in compliance with PRISMA criteria. From 2000 to 2022, we looked for researches in Embase, PubMed, the Cochrane Library and Web of Science. Every study that addressed the impact of APRV on adults suffering from ARDS was included. The oxygenation status was our main outcome. Mortality and the length of stay (LOS) in the critical care unit were the secondary outcomes. *Results:* Six studies were included in this systematic review. Tidal volume was set in 4 to 6 mL/kg in four investigations that evaluated APRV to traditional modes that employ low tidal volume technique. In the other two investigations, tidal volume larger than 6 mL/kg was employed to test APRV to synchronized intermittent mandatory breathing. All trials provided the mortality result; and five studies reported intensive care unit LOS. *Conclusion:* This study concludes that APRV use have shortened the LOS in the critical care unit and boosted oxygenation on day three.

**Keywords:** Mechanical ventilation, acute respiratory distress syndrome, airway pressure release ventilation

## 1. INTRODUCTION

A vital life support strategy for individuals suffering from ARDS is mechanical ventilation (Fan et al., 2017). Nevertheless, it could exacerbate lung injury brought on by repeated alveolar collapse with shearing or localised alveolar overstretch (Kuchnicka and Maciejewski, 2013). Since the development of the low tidal volume (LTV) ventilation strategy two decades ago, several mechanical ventilation (MV) techniques have attempted to mitigate ventilator-induced lung damage while supposing that alveoli respond elastically, within an elastic load limit, due to the interplay between collagen and elastin (Meade et al., 2008; Gattinoni et al., 2010). Alveolar recruitment and collapse, on the other hand, are dependent upon both the duration of pressure exerted on the lung, particularly in the event of lung damage. This is because alveoli function as a viscoelastic system (Allen et al., 2005). Based on the information above, APRV, which was first introduced in 1987, is defined as a continuous positive airway pressure with a brief intermittent release phase.

It is based on the open lung concept and allows the user to independently control inspiratory and expiratory time, allowing for the release of only a partial lung volume and spontaneous breathing throughout the high level of pressure (Lachmann, 1992; Amato et al., 1995). APRV is exclusively utilized as rescue therapy in acute lung injury patients, not in normal clinical practice, despite its theoretically appealing benefits over other traditional mechanical ventilation techniques. APRV regimens have been shown in several trials to improve gas exchange and alveolar recruitment in ARDS patients (Kollisch et al., 2016). A few published clinical trials have evaluated the effectiveness of early APRV administration in ARDS patients to enhance oxygenation and lower mortality, based on observational studies. Nonetheless, there is ongoing debate on the APRV effect in treating patients with ARDS, mostly because of variations in APRV administration and timing of beginning (Carsetti et al., 2019). We aimed to evaluate how well APRV works in improving oxygenation and lowering mortality in adult ARDS patients.

## 2. METHOD

This work is a systematic review carried out in accordance with PRISAM principles (Moher et al., 2009). This study's primary goal was to determine if APRV is more effective than other mechanical breathing techniques at increasing oxygenation in critically sick patients with ARDS. The following databases were searched from 2000 to 2022 for published clinical studies examining the use of APRV in the treatment of adult ARDS patients who were admitted to the intensive care unit: MEDLINE, Embase, Web of Science, and the Cochrane Central Register of Controlled studies database. Included are all clinical trials where APRV was contrasted with any other conventional technique of operation. Crossover studies, observational studies, reviews, and research using experimental animals were not included in our sample.

The relevant articles were defined using a combination of the following keywords: Airway pressure release ventilation, continuous positive airway pressure, and respiratory distress syndrome. We used the reference list and grey literature to look up other publications. Only English-language articles were included. The authors individually carried out the first search and looked through the abstracts and titles to find any papers that could be relevant. Following the start of the mechanical ventilation, the complete text of possibly pertinent articles was evaluated for inclusion based on the recorded oxygenation measurement. Secondary data on duration of stay and death were gathered. The information on the primary and secondary outcomes, the year of publication, the kind of research, the number of patients in the APRV group, the type of conventional mode, and the percentage of patients who died were all extracted using data extraction forms.

## 3. RESULTS

During our first search of the databases, we found 196 citations. Following the elimination of duplicates, we evaluated the entire texts of 65 studies and the abstract and titles of 161 records, finally we included 6 articles in this systematic review (Figure 1) enrolling 375 patients in total (Hirshberg et al., 2018; Zhou et al., 2017; Li et al., 2016; Maxwell et al., 2010; Varpula et al., 2004; Putensen et al., 2001). The primary attributes of the chosen studies are presented in (Table 1). The APRV group's mean age ranged from 40 to 57 years, whereas the conventional mode group's mean age ranged from 42 to 53 years. Tidal Vt was set between 4 and 6 mL/kg in four investigations (Putensen et al., 2001; Maxwell et al., 2010; Zhou et al., 2017; Hirshberg et al., 2018) that evaluated APRV to traditional modes that employ LVT technique. In the other two investigations, Vt larger than 6 mL/kg was employed to test APRV to synchronised

intermittent mandatory breathing. The oxygen saturation was included for the primary result in all research in the tables or figures of the publications.

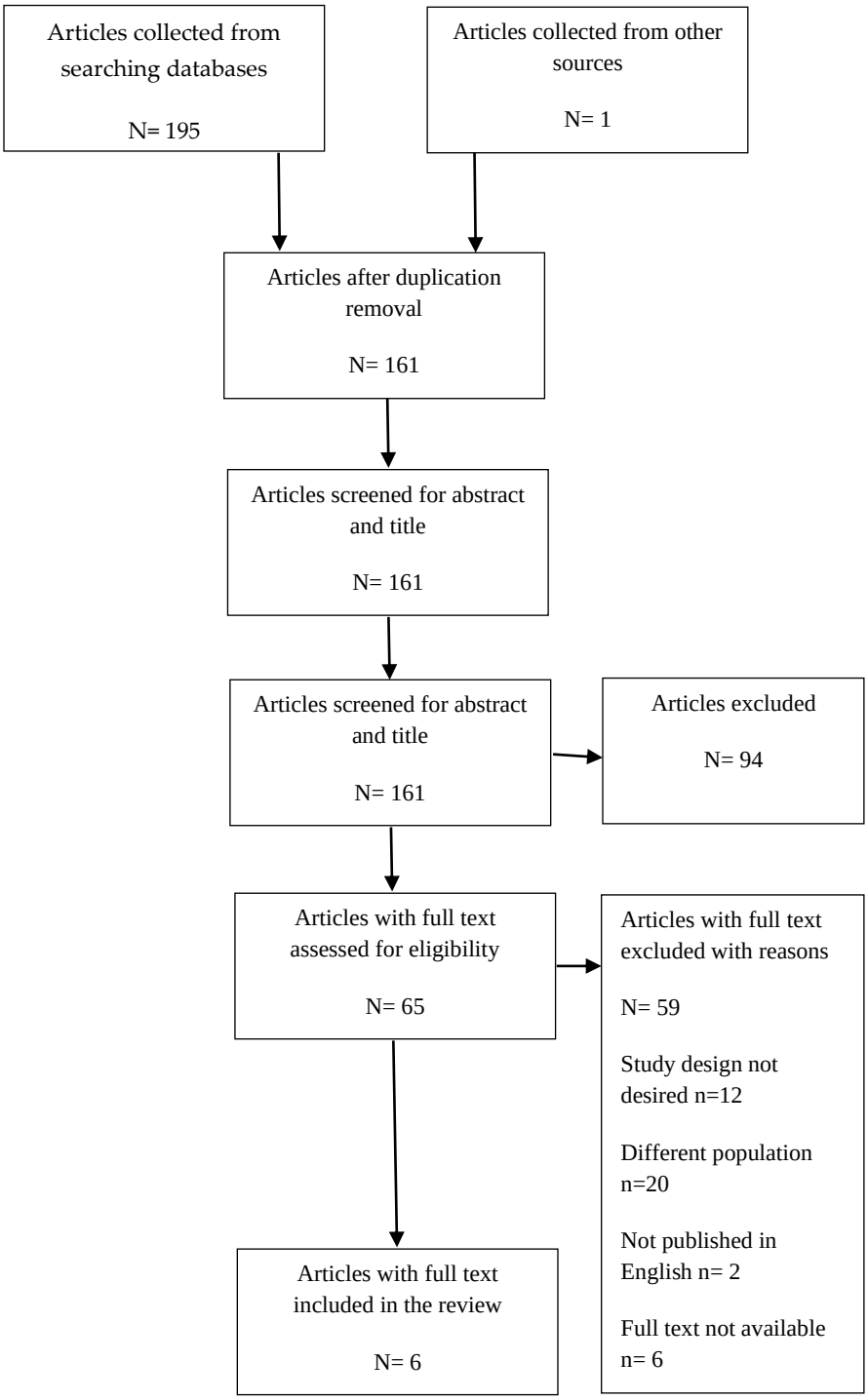


**Figure 1** PRISMA consort chart of selected studies

All trials provided the mortality result; and five studies Putensen et al., (2001), Maxwell et al., (2010), Li et al., (2016), Zhou et al., (2017), Hirshberg et al., (2018) reported the LOS in the ICU. The studies' definitions of ARDS differed; some utilised the Berlin definition, while others followed the guidelines set forth by American-European Consensus Conference on ARDS (Ranieri et al., 2012;

Bernard et al., 1994). According to Putensen et al., (2001) sustaining spontaneous breathing during APRV reduces the sedation need and enhances cardiopulmonary function, most likely by drawing in nonventilated lung units and necessitating a shorter stay in the ICU and ventilatory support. Li et al., (2016) found APRV's conditions have improved in addition to improvements in airway peak pressure, the oxygenation index, lung dynamic compliance, extravascular lung water relief, Murray score and functional residual capacity. Because the researchers were not blinded, there was a substantial bias risk in all of the experiments because to departures from the planned intervention. For the same reason, there was a moderate bias risk in most of the studies when it came to outcome measurement. Main findings of studies included in the review was presented in (Table 2).

**Table 1** Characteristics of studies included in the review

| Study | Sample size | Comparator mode and tidal volume strategy, Vt unit ml/kg | The mean of PaO2/FiO2 after 3 days day 3 in mmHg | The mean of PaO2/FiO2 at zero time in mmHg |
|---|---|---|---|---|
| Hirshberg et al., 2018 | APRV: 17<br>AC–VC: 17 | AC–VC (Vt=6) | APRV: 168<br>AC–VC: 162 | APRV: 109<br>AC–VC: 121 |
| Zhou et al., 2017 | APRV: 71<br>AC–VC: 67 | AC–VC (Vt=6) | APRV: 280<br>AC–VC: 180 | APRV: 121<br>AC–VC: 138 |
| Li et al., 2016 | APRV: 26<br>SIMV–VC: 26 | SIMV–VC (Vt=6–8) | APRV: 220<br>SIMV–VC: 212 | APRV: 119<br>SIMV–VC: 118 |
| Maxwell et al., 2010 | APRV:31<br>SIMV–VC: 32 | SIMV + (PS–VC) (Vt=6) | APRV: 300<br>SIMV-VC: 280 | APRV: 320<br>SIMV–VC: 363 |
| Varpula et al., 2004 | APRV:30<br>SIMV–PC: 28 | SIMV + (PS–PC) (Vt = 8–10) | APRV: 195<br>SIMV–PC: 165 | APRV: 150<br>SIMV–PC: 164 |
| Putensen et al., 2001 | APRV= 15<br>AC–PC=15 | AC–PC (Vt =6) | APRV: 320<br>AC–PC: 175 | APRV: 250<br>AC–PC: 250 |

**Table 2** Main findings of studies included in the review

| Citation | Main findings |
|---|---|
| Hirshberg et al., 2018 | Despite a strategy intended to achieve modest tidal volume ventilation, APRV frequently produced release volumes more than 12 mL/kg. Low tidal volume ventilation objectives cannot be delivered in a consistent or repeatable manner using the APRV procedures currently in use. |
| Zhou et al., 2017 | Patients in the APRV group experienced a greater median number of ventilator-free days in comparison to those in the LTV group. This result held true regardless of the concurrent variations in chronic illness. The duration of the APRV group's ICU hospitalization was reduced. The ICU mortality rate in APRV group was 19.7% while the LTV group mortality rate was 34.3%. This was linked to improved respiratory system and oxygenation compliance, a lower Pplat, and a reduced need for sedation in the first week after enrollment. |
| Li et al., 2016 | APRV's conditions have improved. The results showed improvements in airway peak pressure, the oxygenation index, lung dynamic compliance, extravascular lung water relief, functional residual capacity, and Murray score. |
| Maxwell et al., 2010 | When it comes to patients who have suffered severe trauma and need mechanical breathing for more than 3 days, APRV appear to have comparable safety profiles. Higher scores on the |

| | |
|---|---|
| | Acute Physiology and Chronic Health Evaluation may indicate an early worsening of physiologic derangement, which might account for trends in APRV patients' increased ventilator days, LOS in ICU, and ventilator-associated pneumonia. |
| Varpula et al., 2004 | During the first 7 days of the research, there was a considerable reduction in respiratory pressure in the group undergone APRV. The groups' physiological parameters and PEEP levels were similar. Both the mortality and the number of days without a ventilator were comparable at day 28. |
| Putensen et al., 2001 | Sustaining spontaneous breathing during APRV reduces the need for sedation and enhances cardiopulmonary function, most likely by drawing in non-ventilated lung units and necessitating a shorter stay in the ICU and ventilatory support. |

## 4. DISCUSSION

Protective ventilation techniques are essential for managing patients with ARDS because they prevent lung injury or over distension caused by the alveoli's cyclical opening and shutting. Optimizing gas exchange while lowering the risk of lung damage is possible with the APRV mode. Furthermore, spontaneous breathing made possible by APRV improves functional residual capacity, promotes alveolar recruitment, and lowers the elastic effort of breathing, all of which increase gas exchange (Jain et al., 2016). Three systematic reviews and meta-analyses comparing the effectiveness of APRV to other ventilatory modes in treating patients with ARDS were published in 2019 and 2020 (Carsetti et al., 2019; Lim et al., 2019; Sun et al., 2020). This shows that there is support for managing ARDS with open lung ventilation based on the APRV mode. In the first, published in April 2019, Carsetti et al., (2019) examined the number of days without ventilator among ARDS patients who were intubated and compared the APRV mode to a traditional ventilation approach.

The authors showed a larger number of days without ventilator and a outcomes in patients with ARDS treated using APRV compared to traditional ventilation. Additionally, they observed no difference in oxygen saturation between the traditional ventilatory mode group and the APRV group on day 3, which contradicted the findings of our study. The variance in the pooled estimate of the outcome assessed can be ascribed to the several clinical studies that were incorporated. As a result, only two clinical studies for mortality and three studies for the measurement of oxygen saturation were included by (Carsetti et al., 2019). Six studies were included in our analysis of oxygen saturation and mortality. The disparity between the findings of the two studies can be explained by mortality measurement, which was all-cause mortality.

Reviewing the all-cause death rate was the primary focus of the second meta-analysis research that looked at the effectiveness of APRV in treating patients with ARDS (Lim et al., 2019). When ARDS adult patients were treated with APRV as opposed to traditional breathing techniques, they found a decrease in mortality. Sun et al., (2020) study included studies showed that employing APRV to treat ARDS patients might raise their oxygen saturation. However, because of the variability in the technique, which might have an impact on the validity of the results, a significant drawback of the third investigation was merging the data from observational studies and clinical trials. The outcomes would also be impacted by the various features of the pooled population from the observational research and clinical trials.

APRV has been shown to have numerous physiological advantages when used in patients with ARDS and those at risk of developing ARDS based on clinical evidence. This is because it can enhance oxygenation and hemodynamic function, carry out alveolar recruitment, preserve spontaneous breathing, and reduce lung injury without increasing the side effects on the function of extra pulmonary organs, which is highly consistent with the idea of treating ARDS. Furthermore, APRV is still not widely used in clinical settings due to its complex and non-specific characteristics. Moreover, because there are several ARDS phenotypes, each of which is linked to a unique set of pathophysiological alterations (Cheng et al., 2022).

## 5. CONCLUSION

According to this study, utilizing the APRV mode may have increased oxygenation on day three and decreased the LOS in ICU. Given the constraints of this research, it is important to take into account the impact of heterogeneity of the included studies when interpreting the results.

**Ethical approval**
Not applicable

**Author's contribution**
Mohammed Sagheer Albarqi, Rakan Abdullah Alshareef, Mortada Hassan Aljassas, Ahmed Alsiwar: Participated in introduction and discussion
Saad Alsaad, Mania Salem Al-baqawi, Fahad Bader AlGhounaim: Participated in writing result and method
Kamal Alsofyani: Participated in collecting literature abstract conclusion and submission
Mohammed Sultan Alshehri: Participated in collecting literature, writing abstract conclusion
Faisal Naif Alshammari: Participated in all steps of the research from the idea to the submission

**Abbreviation**
APRV: Airway pressure release ventilation
LOVT: Low tidal volume ventilation
ICU: Intensive care unit
Pplat: Plateau airway pressure
Vt: Tidal volume
LOS: Length of stay
ICU: Intensive care unit
ARDS: Acute respiratory distress syndrome
LTV: Low tidal volume
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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**Conflict of interest**
The authors declare that there is no conflict of interests.

**Data and materials availability**
All data sets collected during this study are available upon reasonable request from the corresponding author.

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